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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/634,039	04/17/96	SNIDER D	1038-588M157

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EXAMINER	
VANDER VEGT, F	
ART UNIT	**PAPER NUMBER**
1644	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/634,039	Applicant(s) Snider et al
	Examiner F. Pierre VanderVegt	Group Art Unit 1644

X Responsive to communication(s) filed on *Jun 22, 1999* .

X This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-9* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

X Claim(s) *1-9* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-9 are pending in this application.

1. The Petition to Correct Inventorship under 37 CFR 1.48(a) filed November. 22, 1996 and Consent of Assignee to Correction of Inventorship filed January. 20, 1997 have been received and duly noted. The intent of these papers is, however, unclear. Both documents authorize a change of inventorship to include only Denis P. Snider to the exclusion of Mark R. McDermott and Brian J. Underdown. The application currently lists Dr. Snider as the sole inventor, evidenced both by the file wrapper and the filing receipt. The original declaration submitted with the specification was not signed and the substitute declaration of November. 7, 1996 was signed only by Denis P. Snider. The names of Mark R. McDermott and Brian J. Underdown were lined through on the substitute declaration of November. 7, 1996. Therefore, Denis P. Snider is already listed as sole inventor and the proposed correction is not necessary.

It is further noted that on his declaration dated November. 5, 1996, that Brian J. Underdown, in item 2, does not consider himself to be an inventor of the claimed invention. On his declaration dated November. 5, 1996, Denis P. Snider, in item 2, claims to be sole inventor of the claimed invention. On his declaration dated November. 5, 1996, Mark R. McDermott, in item 2, also claims to be sole inventor of the claimed invention. This is in conflict with the said declaration of Denis P. Snider and also that of registered representative Michael I. Stewart dated August. 23, 1996.

Clarification and/or correction is required.

The Office recognizes Applicant's intent to submit a new declaration by Mark R. McDermott in order to correct the inventorship of this application. However, this requirement for clarification and/or correction stands until a properly executed document is filed.

Oath/Declaration

2. The oath or declaration remains defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state ~~whether~~ the inventor is a sole ~~or joint~~ inventor of the invention claimed.

The Office recognizes Applicant's intent to submit a new declaration by Denis P. Snider in order to correct the deficiency. However, this requirement for a new oath or declaration stands until a properly executed document is filed

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-6, 8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al (13).

It was previously stated that: "The '480 patent teaches a method to confer protection against pathogenic organisms using monoclonal antibodies (mAbs) specific for membrane determinants expressed on mammalian antigen presenting cells as a targeting moiety which are coupled to antigens derived from pathogenic organisms (Abstract in particular). For example, a peptide from Herpes simplex virus was coupled to an anti-MHC class II mAb and elicited an IgG response (Example IV and Figure 4 in particular). The '480 patent further teaches that this method is helpful in the induction of antigen-specific IgG responses (Abstract in particular). The '254 patent provides the same teachings. The '480 patent and the '254 patent do not teach intranasal administration or a heterobifunctional linking molecule. Wu et al teaches the intranasal administration of *Streptococcus mutans* surface protein antigen I/II (AgI/II) coupled to cholera toxin B subunit (CTB)(Abstract in particular). AgI/II and CTB are coupled through a

heterobifunctional linking molecule (page 315, subsection "Antigens" in particular). Wu et al also teaches that intranasal administration of the AgI/II-CTB complex induced IgG and IgA antibody production better than AgI/II alone (Figure 4 in particular) and required no further adjuvant for a strong salivary IgA response (page 320, first full paragraph in second column in particular) and that antibodies were found in response to the immunization in saliva as well as gut and tracheal washes (Table 1 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to be motivated to combine the teachings of the '480 or '254 patents concerning anti-APC mAb-antigen conjugates with the teachings of Wu et al concerning intranasal administration of antigen to elicit a protective response to pathogenic organisms. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms."

Applicant's arguments filed June 22, 1999 have been fully considered but they are not persuasive.

In response to Applicant's argument that the '480 and '254 patents teach only parenteral administration and do not suggest intranasal administration, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Applicant has offered no specific reasons as to why the '480 and '254 patents would not lead to a reasonable expectation of success on the part of one of ordinary skill in the art. The statement on page 3 of the response filed June 22, 1999, that "*the success in eliciting a good immune response to an antigen by parenteral administration of the antigen-antibody as described in the Barber et al patents is not predictive of obtaining a strong immune response by intranasal administration of the antigen antibody conjugates*" is a mere assertion not buttressed by facts. It is respectfully submitted that Wu et al demonstrates successful immunization to an antigen via an intranasal route and that the combination of Wu et al with the '480 and '254 patents would the artisan a reasonable expectation of success.

5. Claim 7 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al (13) as applied to claims 1-6 and 8 above, and further in view of Dempsey et al (U) and ATCC Catalogue of Cell Lines and Hybridomas, Seventh Edition (V).

It was previously stated that: "The '480 patent, '254 patent and Wu et al have been discussed supra. Wu et al further teaches that the nasal passages of rats and mice contain organized lymphoid tissue that is considered to be the equivalent of Waldeyer's ring in humans and that $CD4^+$ T cells (which are crucial in establishing an antigen-dependent immune response) outnumber $CD8^+$ T cells among intraepithelial and submucosal lymphocytes of nasal mucosae in humans (page 320, first paragraph of Discussion in particular). The combination of references does not teach a monoclonal antibody to human APCs. Dempsey et al teaches that conjugation of antigen to complement component C3d, which binds to CD21 on B cells, results in the production of antibodies to said antigen without addition of any additional adjuvants (see entire document, Figure 4 in particular). The ATCC catalogue offers for public sale the hybridoma which produces the anti-human C3d receptor (CD21) monoclonal antibody THB-5 (page 364, ATCC HB 135 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the THB-5 anti-human CD21 mAb for the anti-mouse mAb of the '480 or '254 patents and combine the teachings of the '480 patent concerning anti-APC mAb-antigen conjugates with the teachings of Wu et al concerning intranasal administration of antigen to elicit a protective response to pathogenic organisms. One would have been motivated, with a reasonable expectation of success to combine these teachings based on the teachings of Wu et al of similarities between the tissues of the nasal passages of humans and rodents and the high proportion of $CD4^+$ T cells in these tissues, the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and the ease of purification of a mAb from an established hybridoma cell line rather than isolation and purification of a complement component."

Applicant's traversal of the application of the '480 and '254 patents and Wu et al has been discussed supra. Applicant has further traversed the addition of the Dempsey et al reference on the grounds that Dempsey et al teaches only interperitoneal administration. This is not found persuasive because the antibody-antigen conjugate taught by Dempsey et al can easily be substituted for the conjugate taught by the '480 and '254 patents and used intranasally based upon the aforementioned combination of the '480 or the '254 patent with Wu et al.

6. Claim 9 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al, U.S. Patent 4,950,480 (A), or Barber et al, U.S. Patent 5,194,254 (B), each in view of Wu et al

(13),, as applied to claims 1-6 and 8 above, further in view of Babington, U.S. Patent 4,228,795 (C).

It was previously stated that: "The '480 patent, '254 patent and Wu et al have been discussed supra. The combination of references does not teach a disperser for dispersing an aerosol. The '795 patent teaches a nebulizer which can be used to aerosolize mendicants for nasal inhalation (Figure 4 and column 6, line 7 through column 8, line 54 in particular). The '795 patent further teaches that said nebulizer is suitable for use with viscous or sticky substances (column 8, lines 34-37 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the nebulizer taught by the '795 patent to administer the mAb-pathogenic antigen conjugate taught by the combination of the '480 or '254 patents with Wu et al intranasally. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and by the teachings of the '795 patent that the nebulizer is usable with sticky substances, which a common property of proteinaceous solutions."

Applicant's traversal of the application of the '480 and '254 patents and Wu et al has been discussed supra. Applicant has not provided any further specific arguments regarding the applicability of the '795 patent. Accordingly, this ground of rejection stands without any further comment.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and even-numbered Mondays (on 1999 365-day calender) from 7:00 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
September 13, 1999

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PRIMARY EXAMINER
ART UNIT 182 1644